26

Claims

35

- 1. An immortalized hepatocyte cell culture of human normal cell origin retaining an enzyme activity involved in the metabolism of xenobiotics in the liver or the capability of expressing a gene encoding an enzyme involved in the metabolism of xenobiotics in the liver.
- 2. The cell culture according to Claim 1 wherein the enzyme activity is NADPH cytochrome P450 reductase activity, activity, ethoxyresorufine glucuronosyl transferase 10 dealkylation activity, benzyloxyresorufine dealkylation pentoxylresorufine dealkylation activity, activity, flavin dealkylation activity, methoxyresorufine hydratase activity, epoxy activity, monooxygenase sulfotransferase activity or glutathione S-transferase 15 activity.
 - 3. The cell culture according to Claim 1 wherein the enzyme is NADPH cytochrome P450 reductase, NADPH cytochrome P450, flavin monooxygenase, epoxy hydratase, glucurosyl
- transferase, sulfotransferase or glutathione S-transferase.

 4. The cell culture according to Claim 3 wherein the NADPH cytochrome P450 is CYP1A1, CYP1A2 or CYP3A.
 - 5. The cell culture according to Claim 1 wherein the cell culture is FERM BP-6328.
- 6. A method of producing the cell culture according to Claim 1, characterized by introduction of the T antigen gene of SV (simian virus) 40 origin into human normal hepatocytes.
- 7. The production method according to Claim 6 wherein the human normal hepatocytes are hepatocytes of human fetal origin.
 - 8. A screening method for a compound or a salt thereof ① which inhibits or promotes an enzyme activity involved in the metabolism of xenobiotics in the liver or ② which inhibits or promotes the expression of a gene encoding an enzyme involved in the metabolism of xenobiotics in the

liver, characterized by the use of the cell culture according to Claim 1.

- 9. A compound or a salt thereof ① which inhibits or promotes an enzyme activity involved in the metabolism of xenobiotics in the liver or ② which inhibits or promotes the expression of a gene encoding an enzyme involved in the metabolism of xenobiotics in the liver, obtained by using the screening method according to Claim 8.
- 10. An analytical method for (a) enzymes involved in the metabolism of xenobiotics and/or endogenous substrates, (b) metabolic pathways for xenobiotics and/or endogenous substrates, (c) chemical structures of metabolites of xenobiotics and/or endogenous substrates, (d) inhibition of enzymes which metabolize xenobiotics and/or endogenous substrates, (e) promotion of the activity of enzymes which 15 metabolize xenobiotics and/or endogenous substrates, (f) cytotoxicity due to the metabolism of xenobiotics and/or (g) genotoxicity due substrates, endogenous the metabolism of xenobiotics and/or endogenous substrates, (h) carcinogenicity due to the metabolism of xenobiotics and/or 20 substrates, (i) mutagenicity due the endogenous metabolism of xenobiotics and/or endogenous substrates, (j) hepatotoxicity due to the metabolism of xenobiotics and/or endogenous substrates, or (k) hepatic action of xenobiotics and/or endogenous substrates, characterized by the use of 25 the cell culture according to Claim 1.
 - 11. A method of preparing metabolites of xenobiotics and/or endogenous substrates, characterized by the use of the cell culture according to Claim 1.